REMARKS

The issues outstanding in the office action of May 7, 2010, are the rejections under 35 U.S.C. 112 and 103. Reconsideration of these issues, in view of the following discussion, is respectfully requested.

At the outset, for clarity of the record, it is noted that the office action states, at page 2, that applicants "have filed no amendment or response with the Request for Continued Examination." In fact, applicants filed an Amendment Under 37 C.F.R. 1.116 in response to the final rejection, which amendment was not entered (see the Advisory Action dated March 11, 2010) and applicants' Request for Continuing Examination filed March 26, 2010, presented, as a submission under 37 C.F.R. 1.114, a request to consider the amendments in the February 26 reply. See item 1(a)(i) on the Request for Continuing Examination.

Rejections Under 35 U.S.C. 112

The Examiner is thanked for indicating withdrawal of the previous rejection under 35 U.S.C. 112. Claims 5 and 7-11 are now rejected under 35 U.S.C. 112, second paragraph. It is argued, at page 2 of the office action, that it is not possible to determine what is meant by decellularization even in "deep" interior portions. While it is argued that the term "deep" is not defined in the specification, this is respectfully submitted to be inaccurate. Paragraph 24 of the specification, referencing figure 2, states that the photograph which is figure 2 represents decellularization "even in deep interior portions" while paragraph 11, also discussing the photograph which is figure 2, states that, in the figure, "residual nuclei are observed in the interior of the tissue treated with the prior art solution alone". Thus, it is submitted that it is clear that decellularization in "deep" interior portions means that there are no residual cellular nuclei on histological examination as performed in figure 2, i.e., histological examination of hematoxylin-eosin stained tissue. See paragraph 23 of the specification detailing such evaluation ("HE" refers to staining with hematoxylin and eosin.)

Accordingly, it is submitted that the claim is now even further clear to one of ordinary skill in the art, and withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. 103

Claims 5 and 7-11 remain rejected under 35 U.S.C. 103 over Login taken with Giberson and Boon. Reconsideration of this rejection is again respectfully requested. Login discloses a process employing microwave irradiation along with a physiologic salt solution or a dilute aldehyde solution, to preserve tissue in the preparation of bioprosthesis for implantation into patient. In the method of Login et al., a specimen of biological tissue is immersed in an osmotically balanced solution (OBS). The purpose of utilizing OBS is to *prevent the loss* of important cellular constituents due to diffusion. See, col. 5, lines 9-11. This is consistent with "tissue fixing" e. g. by exposure to glutaraldehyde or formaldehyde, note the discussion of cell fixing at column 2, along 31-33 and lines 52-53 patent. Such "fixing" is *not* decellularization in the deep interior of the tissue, i.e., so that there are no residual cellular nuclei. Treatment or immersion a solution such as osmotically balanced solution does not enable removal of cellular components, even with the microwave radiation treatment of the patent. In Login's method, the tissue immersed in OBS initially at room temperature (approximately 20°C) is irradiated with microwave energy at a sufficient does and for a sufficient time such that the temperature of the solution is within the range of 35°C to 50°C. This time is short, e.g. between one and fifty seconds. See, e.g. claim 6. Thus, Login does not disclose a process which can result in interior decellularization as claimed..

In the present invention, the tissue immersed in the treating solution is irradiated with considerably greater intensity, e.g., with microwaves at a frequency of 2450MHz (the frequency of a standard microwave oven) for a net period of time so as to achieve complete decellularization or for at least 1 hour while maintaining the temperature in the range of 0°C to 40°C, (see Claim 10). The duration of microwave irradiation in Claim 10 is at least 72 times greater than the duration of microwave irradiation of Login's method. Moreover, in Login, the microwave oven will be automatically shut off when the pre-set final irradiation temperature of the solution is obtained (col. 4, lines 65-67). In other words, Login never irradiates the tissue specimen in OBS with microwave energy at a dose and for a length of time such that temperature of the solution reaches above patentees' preset temperature of 35°C to 50°C. Such duration of microwave irradiation is not sufficient to achieve deep interior decellularization, e.g., so that no

residual nuclei are detected on histological examination. With a large enough dose of microwave energy to remove cellular membrane and release intracellular components, such as in the present invention, it is necessary to cool the tissue in the treating solution to maintain the generating temperature from 0˚C to 40˚C as recited in the claims.

In addition, the disclosure of Login is simply does not suggest to one of ordinary skill, particularly in the absence of a decellularizing chemical, complete decellularization and/or the conditions recited in the present invention. The osmotically balanced solutions (OBS) of Login et al. are free of any decellularizing chemical such as the presently recited detergents and, therefore, are not capable of decellularizing native biological tissues.

In Giberson a tissue specimen is immersed in a formalin based solution, and irradiated with microwaves. Formalin is well known as a fixation chemical of biological tissues for microscopic inspection. Since the morphological characterisitics of the tissue specimen must be preserved for diagnostic purposes, Giberson does not remove any cellular component from the tissue. Boon teaches the use of alcohol or glutaraldehyde as an immersion fluid (page 7, lines 51-55) when irradiating tissue with microwaves. Thus, again, only fixation is taught, and not complete decellularization. These secondary references accordingly do nothing to remedy the deficiencies of Login, and even in combination do not suggest the present claims.

In summary, the present invention applies microwave energy to tissue immersed in a treating solution containing a detergent. The treating solution of Login, with or without glutaraldehyde are not detergents. Boon teaches the use of alcohol or glutaraldehyde as immersion fluids, and Giberson teaches the use of non-formalin fixatives such as aldehydes, alcohol, acetone, Prefer^{tm}, Preserve^{tm}, Glycofixx, SafeFix, etc., see col. 4, lines 5-7 and 45-46. The first four chemicals are clearly not detergents, the other fixatives are identified as "fixatives" not as detergents. A "fixative" is an agent for fixation of tissue, as known in the art, whereby tissue proteins and other cellular constituents are stabilized to withstand processing (see col. 1, lines 39-43 of Giberson). Thus, such fixation would not remove biological components from the tissue, at least, not in a manner as presently claimed. Such fixatives thus even in combination with Login do not remedy the deficiencies of the combination of references.

Accordingly, it is submitted that the rejection under 35 U.S.C. 103 should be withdrawn. The same is respectfully requested.

The claims of the application are submitted to be in condition for allowance. However, if the Examiner has any questions or comments, he or she is cordially invited to telephone the undersigned at the number below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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